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Project No. 408678

Ms. Diane M. Leber
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Dear Diane:

In our conversation with Frank Battaglia on March 9, he requested that IT provide further explanation of the selection process for toxicity values presented in Table X-44 of the November 1991 RFI Interim Report. Enclosed are explanations of the selection of surrogate compounds for the chemicals presented in Table X-44. This information can be used by EPA Region I to aid in their review of the November Report. If you have any questions or comments, please call Tom or myself.

Sincerely,

OK

Mary Swanson
Risk Management Services

cc: Dr. Martin Bernstein
Dr. Tom Marshall
Frank Eidson
Frank Battaglia



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Selection of Surrogate Toxicity Values

The Table X-44 in the November, 1991 interim report lists certain risk assessment factors for analytes in soil or sediment samples taken in Phase I sampling studies. Several of these analytes have insufficient toxicity information, so toxicity values from structurally or chemically similar compounds were substituted, as described in the report. The selection of surrogate chemicals was based on one or more of the following:

- similar toxic effects
- common pathways of metabolism
- structural similarities.

The rationale for surrogate selection is described below for various chemical classes using examples.

Polycyclic Aromatic Hydrocarbons (PAHs)

Benzo(a)pyrene was used as a surrogate for benzo(a)anthracene, benzo(b)fluoranthene, benzo(k)fluoranthene, chrysene, dibenz(a,h)anthracene, and indeno(1,2,3-c,d)-pyrene. Most of these compounds have a bay region, a site of epoxidation and hydroxylation that is common to many carcinogenic PAHs (Williams and Weisburger, 1991). Benzo(k)fluoranthene does not have a bay region, but is nonetheless classified as a B2 carcinogen without quantitative reference doses, reference concentrations, or a slope factor given in EPA's current Integrated Risk Information System (IRIS) database (U.S. EPA, 1992). Therefore, the quantitative data on benzo(a)pyrene was also used for benzo(k)fluoranthene. OK

Chlorinated Aromatic Compounds

2,4-Dichlorophenol was used as a surrogate for 2,6-dichlorophenol. Both compounds are phenols that can be metabolized by conjugating enzymes to form O-glucuronides (Sipes and Gandolfi, 1991). Phenols can also be detoxified by the action of aryl sulfotransferases to form sulfate esters; however, this reaction has a lower capacity than the glucuronidation reaction. Chlorinated aromatic compounds are subject to the action of glutathione S-transferases. OK

Alkyl Benzenes

Ethylbenzene was used as a surrogate for dimethylphenethylamine. Both compounds are expected to be metabolized as alkyl benzene compounds following oxidative deamination of the latter by cytochrome P-450-containing monooxygenases (Andrews and Snyder, 1991). OK

Chlorinated Pesticides

In the absence of specific data for Endosulfan I or Endosulfan II, the chronic RfD for endosulfan was used. Since Endosulfan is usually produced as a mixture of these stereoisomers, it is probable that the RfD reported was based on studies using an isomer mixture. OK

Organophosphorus Pesticides

Methyl parathion was used as a surrogate for famphur. Both compounds are organophosphorous diesters and both are cholinesterase inhibitors. OK

Halogenated Aliphatic Compounds

Bromomethane was used as a surrogate for iodomethane since both compounds are expected to be metabolized by glutathione S-alkyl transferase, produce no liver damage, and cause slight fat accumulation in liver (Andrews and Snyder, 1991).

OK

Nitro-substituted Compounds

Nitrobenzene was used as a surrogate for 2-,3- and 4-Nitroaniline as well as 4-nitrophenol. These compounds are similar in structure and can cause methemoglobinemia and/or Heinz Bodies in the blood (Smith, 1991).

OK

REFERENCES

Andrews, L.S., and R. Snyder, 1991. "Toxic Effects of Solvents and Vapors" in: Casarett and Doull's Toxicology, The Basic Science of Poisons, Fourth Edition. M.O. Amdur, J. Doull, and C. D. Klaassen, eds. Pergamon Press, New York, 1991.

Sipes, I.G., and A. J. Gandolfi, 1991. "Biotransformation of Toxicants" in: Casarett and Doull's Toxicology, The Basic Science of Poisons, Fourth Edition. M.O. Amdur, J. Doull, and C. D. Klaassen eds. Pergamon Press, New York, 1991.

Smith, R. P., 1991. "Toxic Responses of the Blood." in: Casarett and Doull's Toxicology, The Basic Science of Poisons, Fourth Edition. M.O. Amdur, J. Doull, and C. D. Klaassen, eds. Pergamon Press, New York, 1991.

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